

AI The assays for caspase inhibition are based on the cleavage of a fluorogenic substrate by recombinant, purified human Caspases -1, -3, or -8. The assays are run in essentially the same way as those reported by Garcia-Calvo et al. (*J. Biol. Chem.* **273** (1998), 32608-32613), using a substrate specific for each enzyme. The substrate for Caspase-1 is Acetyl-Tyr-Val-Ala-Asp-amino-4-methylcoumarin (SEQ ID NO:1). The substrate for Caspases -3, and -8 is Acetyl-Asp-Glu-Val-Asp-amino-4-methylcoumarin (SEQ ID NO:2).

REMARKS

Applicant has amended the specification at the paragraph spanning pages 76-77 in response to the October 15, 2002 Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

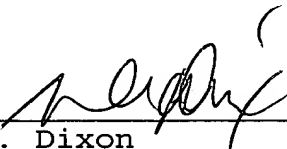
Specifically, applicant has amended to the specification at page 77, line 6 and page 77, line 7 refer to SEQ ID No:1 and SEQ ID No:2, respectively. Applicant has submitted herewith an Appendix of Amendments (Exhibit 1), showing these amendments. In the Appendix, the added portions are underlined and the deleted portions are bracketed.

None of these amendments adds new matter.

Conclusion

Applicant requests that the amendments presented herein be entered, the foregoing remarks considered, and a favorable Office Action be issued.

Respectfully submitted,



Lisa A. Dixon
Attorney for Applicant
VERTEX PHARMACEUTICALS INCORPORATED
130 Waverly Street
Cambridge, Massachusetts 02139-4242
Telephone: (617) 444-6396
Facsimile: (617) 444-6483

EXHIBIT 1

Appendix of Amendments

The assays for caspase inhibition are based on the cleavage of a fluorogenic substrate by recombinant, purified human Caspases -1, -3, or -8. The assays are run in essentially the same way as those reported by Garcia-Calvo et al. (*J. Biol. Chem.* 273 (1998), 32608-32613), using a substrate specific for each enzyme. The substrate for Caspase-1 is Acetyl-Tyr-Val-Ala-Asp-amino-4-methylcoumarin (SEQ ID NO:1). The substrate for Caspases -3, and -8 is Acetyl-Asp-Glu-Val-Asp-amino-4-methylcoumarin (SEQ ID NO:2).